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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/847,102	05/01/2001	Dennis A. Carson	220002062900	5759

7590 10/18/2004

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EXAMINER	
YU, MISOOK	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 10/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/847,102	CARSON ET AL.	
	Examiner	Art Unit	
	MISOOK YU, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 August 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,16,28 and 29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,16,28 and 29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *08/06/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 08/03/2004 has been entered. Claims 1, 5, 16, and 28 are amended. Claims 1-8, 16, 28, and 29 are pending and examined on merits.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

This Office action contains new ground of rejection.

Claim Rejections - 35 USC § 112, Withdrawn

The rejection of claim 5 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in view of the amendment.

Claim Rejections - 35 USC § 103, Withdrawn

The rejection of claims 1-8, 16, 22, 28, and 29 under 35 U.S.C. 103(a) as being unpatentable over any one of Tanaka et al (IDS, #1711998, Proc. Natl. Acad. Sci. USA. vol. 95, pages 10164-9), He et al (IDS # 93, 1997, Science vol. 275, pages 1652-4), or Wang et al (IDS #184, 1996, J. Biol. Chem. vol. 271, pages 4468-76) in view of Campbell, A. (1986, Monoclonal antibody technology, chapter 1 only, Elsevier Science Publishers B.V., Netherlands) is withdrawn in view of the amendment.

The Following Are New Grounds of Rejection

Claim Rejections - 35 USC § 112

Claims 1-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the limitation "the malignant cell" in line 4. There is insufficient antecedent basis for this limitation in the claim. Amending the claim to "a malignant cell" in line 4, followed by "the malignant cell" in line 5 would obviate this rejection. This rejection affects all dependent claims.

Claims 1-8, 16, 28, and 29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is new matter rejection.

This new matter rejection is made because of the new limitation "the antibody inhibits growth of a malignant cell that expresses the frizzled 5 receptor" in the newly amended claims 1, and 16, the new limitation "wherein the antibody is effective for immunotherpay of a malignant cell that overexpresses the frizzled 5 receptor" in claim 28.

Applicant states that the support for the amendment is found at pages 21, 22, 25, and 26. However, the specification at page 21, and 25 discloses expression pattern of

frizzled 2, and frizzled 5 detected by RT-PCR. The specification at page 22 discloses cell growth inhibition with an antibody binding to a frizzled receptor, but does not disclose "the antibody inhibits growth of a malignant cell that expresses the frizzled 5 receptor". The specification at page 26 discloses the effect of an anti-frizzled 2 antibody on growth of cancer cells, not the effect of an anti-frizzled 5 antibody on growth of a malignant cell that expresses the frizzled 5 receptor. This rejection affects all dependent claims.

Claims 1-8, 16, 28, and 29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are interpreted as drawn to an antibody binding to SEQ ID NO:68, or pharmaceutical comprising said antibody, wherein said antibody inhibits growth of a malignant cell that expresses the frizzled 5 receptor.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and

8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The specification discloses that in comparison to normal epithelial cells, all HNSCC had markedly increased mRNA levels of frizzled-2. Treatment of one HNSCC cell line (SNU 1076) with an anti-frizzled 2 antibody inhibited proliferation and induced apoptosis in these cells (note Figs 4, 6, and Example 3).

The specification does not teach whether an anti-frizzled 5 antibody would inhibit growth of a malignant cell that expresses the frizzled 5 receptor. However, Rhee et al., (Sep. 26, 2002, Oncogene vol. 21, issue 43, pages 6598-605) teach at page 6599, left column, under the heading *Expression of Wnt and Fz mRNAs in HNSCC* that "When compared to the housekeeping gene G3PDH, all the Wnts, as well as Fz-2, were expressed more frequently in HNSCC than in normal cells, while there was no difference in Fz-5 gene expression". This suggests that the frizzled 5 receptor might not be expressed on a malignant cell. Note some of authors of the peer-reviewed journal article are the inventors of the instant application.

As for claims 16, and 29 reciting pharmaceutical and claim 28 reciting "effective for immunotherapy", Rhee et al., which was published two years after the instant application had been filed, discloses at page 6599, left column that "the Wnt and Fz genes are frequently overexpressed in HNSCC, and might be attractive targets for both immunotherapy and drug therapy." This suggests that some Wnt and Fz genes overexpressed in HNSCC might be attractive targets for both immunotherapy and drug therapy. This indicates that frizzled 5 receptor which is not overexpressed in those

cancer cell lines tested does not appear to be a good target for immunotherapy or drug therapy. Further, even those frizzled genes that are overexpressed in the tested cancer cell lines, pharmaceutical development is a way in the future. In other words, a pharmaceutical against frizzled receptor overexpressed has not been developed yet. Inherent in pharmaceutical is in vivo use. The specification does not teach any antibody to instant SEQ ID NO:68 capable of treating any disease. Based on Rhee et al., one of skilled in the art has to screen a large clinical samples to see which malignant cell expresses the frizzled 5, followed by screening for an anti-frizzled 5 antibody capable of binding instant SEQ ID NO:68 that inhibits growth of a malignant cell or is effective. The specification has not even established whether frizzled 5 receptor overexpresses in any in vivo malignant cell as compared to normal healthy control, nor does the specification teach a single species of a purified antibody that binds to an extracellular domain of a frizzled 5 receptor, wherein the antibody inhibits growth of a malignant cell that expresses the frizzled 5 receptor.

It is noted that law requires that the disclosure of an application shall inform those skilled in the art how to make the alleged discovery, not how to screen it for them.

Considering the unpredictable state of art, limited guidance, no examples in the specification how to use the instantly claimed invention, broad breath of the claims, it is concluded that undue experimentation is required to practice the invention.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MISOOK YU, Ph.D. whose telephone number is 571-

272-0839. The examiner can normally be reached on 8 A.M. to 5:30 P.M., every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey C Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MISOOK YU, Ph.D.
Examiner
Art Unit 1642